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ABSTRACT

Cyclosporin and Alternative Cyclical Immunosuppressants in Psoriasis

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With the introduction of cyclosporin as the parent molecule of a whole new class of immunosuppressants, a fundamental change in the management of a series of dermatological disorders has ensued. Not only psoriasis, but also atopic dermatitis, pyoderma gangrenosum, morbus Behçet, actinic reticuloid and lichen ruber planus have been found to be responding. Cyclosporin is a cyclic peptide that, together with cyclic lactones, forms a new class of cyclic immunosuppressants. Their precise mechanism of action is as yet not defined, and may differ from molecule to molecule. It seems evident that they interact with cytokine production regulation at the genetic level and intercept T-cell production of IL-2, IFN-τ, IL-4 and IL-5.

The molecular weight of cyclic immunosuppressants is generally well over 500 D, which makes their possible use as topical agents highly unlikely, perhaps with the exception of application on non-cornified mucous membranes. Cyclosporin is registered for severe psoriasis in many countries and is tolerated reasonably well by a subgroup of patients. Dosage usually starts at 3 mg/kg/day, and it is advised to use cyclosporin as part of rotational therapy in psoriasis patients. Side effects of major concern are nephrotoxicity, development of hypertension, and possible facilitation of malignancies, especially squamous cell carcinoma, in patients who have received high dosages of photo-(chemo)therapy. In view of the benefit/risk ratio, that is now well established in psoriasis, alternative therapies with other cyclic immunosuppressants are under development.

IMM-125 is a cyclosporin-derivative with a certain anti-psoriatic effect, but the number of patients studied thus far is limited. FK-506 (tacrolimus) is a cyclic lactone that has proved efficacious when given systemically to patients with psoriasis and with pyoderma gangrenosum. Again, its risk/benefit ratio remains to be precisely defined. Alternative cyclic immunosuppressants such as desoxy-spergualin, tetranactin, didemnin-B and others have as yet not been investigated in dermatology.

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